Wyeth Pharmaceuticals

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July 1, 2005

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2005N-0157: Agency Information Collection Activities; Proposed Collection; Comment Request; Postmarketing Adverse Drug Experience Reporting (70 Federal Register 22882, May 3, 2005)

Dear Sir/Madam:

Wyeth Pharmaceuticals is submitting the following comments in response to the above referenced notice announcing an opportunity to comment on the proposed collection of information related to postmarketing adverse experience reporting. Wyeth is one of the largest research-based pharmaceutical and healthcare products companies and is a leading developer, manufacturer and marketer of prescription drugs, biopharmaceuticals, vaccines, and over the counter medications.

Wyeth appreciates the opportunity to provide comments on the reporting and recordkeeping requirements for postmarketing adverse drug experiences (21 CFR 310.305 and 21 CFR 314.80). Comments are formatted in accordance with the questions posed in the May 3, 2005 Federal Register notice.

1. Is the proposed collection of information necessary for the proper performance of FDA's functions, including whether the information will have practical utility?

- We agree that the collection of adverse event (AE) information, both expedited and Periodic Reports, is necessary and has practical value in monitoring the safety of marketed products.

2. Are FDA's estimates of the burden of the proposed collection of information, including the validity of the methodology and assumptions used, accurate?

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- It is not clear what methodology and assumptions were used by FDA to calculate either the annual reporting burden or the annual recordkeeping burden of the proposed collection of information.

- The FDA estimates of the burden of AE reporting for 15-Day Alerts, Periodic Reports and recordkeeping seem grossly underestimated, as discussed in further detail below.

- Citations 310.305 (c) (5) and 314.80 (c) (1) (iii) in the first two rows of Table 1 refer to drugs without approved marketing applications, and non-applicants, respectively, rather than applicants. The citations used for rows 1 and 2 of this table should be 314.80 (c) (1) (i) and (ii), which refer to the requirements for submission of initial and follow-up 15-Day Alert reports by the holders of approved marketing applications (or additional rows should be added to the table to include these additional reporting requirements). This discrepancy may account for the apparent underestimation of number of respondents and annual frequency of responses (see next bullet point).

- Wyeth submitted 6,107 15-Day Alert reports to the FDA in 2004. The contribution of Wyeth alone exceeds the total burden reported in Table 1 reinforcing our comment in the second bullet point that the reporting burden is grossly underestimated.

- It is difficult to comment on the reporting burden for Periodic Reports; however, the annual frequency per response, which we assume to be the average number of Periodic Reports submitted per company was estimated to be 20, which is considerably less than the 218 Periodic Reports submitted by Wyeth alone in 2004.

- The estimate of the hours required to prepare each Periodic Report is underestimated and only seems to reflect the time needed to compile the report and write the narrative sections. It does not reflect the additional time that is required to collect, prepare, solicit and process follow-up information for each individual 3500A report. Wyeth estimates that these activities take approximately 90 minutes per each 3500A. A true estimate

of the hours to prepare a Periodic Report should include at least an additional 1.5 hours for each non-15-Day report that is contained within each Periodic Report.

- We do not understand how the annual frequency, total annual reports and total hours are calculated for the estimated annual recordkeeping burden. We need to store each individual 15-Day Alert report, each individual non-15-Day 3500A and each individual Periodic Report. The numbers seems to reflect that each company has one document to store. As one company annually submitting > 6,000 15-Day Alert reports, > 200 Periodic Reports with many thousands of non-15-Day 3500A reports, we can assure the FDA that we spend well over the one hour allotted to each company for these activities.

- Wyeth strongly disagrees with the statement that there are no capital costs, operating, or maintenance costs associated with the collection of 15-Day Alert and Periodic Reports. Wyeth and other pharmaceutical companies develop and maintain or purchase expensive, validated databases to collect and process adverse event information. These systems must continually be enhanced to accommodate new regulatory initiatives, such as the electronic submission of individual case safety reports in accordance with the ICH E2B specifications. Companies must purchase servers (sometimes multiple servers worldwide) and each employee needs hardware and software. Support services for these systems are also quite expensive. Additionally, companies must license MedDRA each year to meet the international standards for common reporting terminology. Costs for computer systems vary widely, but can amount to millions of dollars per year, especially for larger companies. Capital and operational expenses for Wyeth's safety database average $7.6 million per year.

- With regard to the estimated annual recordkeeping burden, we also question the statement that there are no capital, operating, or maintenance costs associated with maintaining records of adverse experience reports for ten years. Companies must maintain facilities to store what amounts to large volumes of paper records, in addition to back-up records on other media (scanned optical images, microfilm, etc.). Costs for storage and retrieval vary widely, depending on the volume of records, rental fees, transportation costs, and retrieval fees, but can be substantial (e.g.,

thousands of dollars per year). Wyeth's storage and retrieval expenses are approximately $22,000 per year.

3. Ways to enhance the quality, utility, and clarity of the information to be collected

- It is important for the FDA to move quickly to change their Periodic Reporting requirements to be consistent with the ICH Guidelines for Periodic Safety Update Reports. This will enable companies to submit the same report to all regulatory authorities globally, and will decrease the burden involved with preparing unique Periodic Reports specifically for FDA. Additionally, for those companies who have received a waiver from the Agency to submit Periodic Reports in the PSUR format, this would decrease the burden of adding US-specific appendices to the reports.

- Periodic Safety Update Reports to the FDA should not routinely include any information in addition to that included in the ICH Guidelines for Periodic Safety Update Reports. Specifically, the FDA should not require full copies in either paper or electronic form of cases that were not subject to expedited reporting. If a potential signal arises about a specific product, the FDA has the authority and opportunity to request all available information associated with any individual case(s).

- Greater collaboration between FDA and companies when FDA identifies a potential signal would facilitate better pharmacovigilance. For example, case reports should be shared and mutually discussed.

4. Ways to minimize the burden of the collection of information on the respondents.

- Electronic submission of 15-Day Alert Reports would decrease the reporting burden. It is important that FDA requirements for electronic submission be harmonized with EMEA requirements, so pharmaceutical companies do not have to develop and validate separate programs.

- Cost savings could be realized by both FDA and companies by eliminating the requirement for submitting original literature articles as

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attachments to 15-Day Alert Reports. Articles would always be available to FDA on request. Alternatively, if there was electronic reporting, the literature article could be submitted electronically as an attachment in accordance with the ICH E2B guidance.

- Cost savings could also be realized by eliminating the requirement to collect non-serious labeled events. Costs associated with collecting information that has little, if any, value has a substantial financial impact on both companies and the Agency.

- We are supportive of FDA's efforts to consider provisions for alternate methods of data storage other than through hard copy paper records. Companies would like the option to choose and maintain methods for storage and retrieval of records according to the individual company's needs. Storing scanned optical images of records instead of paper copies would considerably decrease the need for large file rooms, extensive off-site storage facilities, and the costs associated with maintaining these facilities.

Thank you for the opportunity to comment on this important matter.

Sincerely yours,

Roy J. Baranello, Jr.
Assistant Vice President,
Worldwide Regulatory Affairs